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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/598,826	09/12/2006	**Quanzhi Liu**	089210-000100US	1852

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TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

EXAMINER	
RICCI, CRAIG D	

ART UNIT	PAPER NUMBER
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/598,826	LIU ET AL.	
	Examiner	Art Unit	
	CRAIG RICCI	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 December 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,13,25 and 26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2, 13 and 25-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. The amendments filed 12/23/2008 were entered.

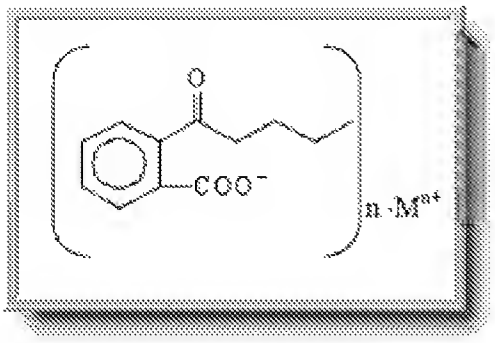
Response to Arguments

2. Applicants' arguments, filed 12/23/2008, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

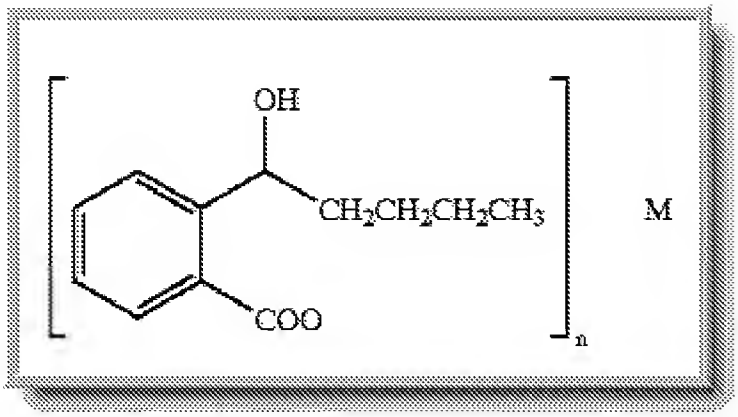
Claim Rejections - 35 USC § 103

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. **Claims 1-2, 13 and 25-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Berge et al* (cited in a previous Action) and *Yang et al* (cited in a previous Action)**.

5. Instant claims 1-2 and 13 are drawn to compounds having the formula  wherein n is 1 or 2 and M is elected as the monovalent metal ion Na^+ which encompasses the compound 2-(α-n-pentanonyl)benzoate. In the previous Action mailed on 09/24/2008, the sodium salt of 2-(α-n-pentanonyl)benzoate was rejected as being unpatentable over STN Registry No. 550-37-8 based on the teaching of *Yang et al* and *Berge et al*. Specifically, over STN Registry No. 550-37-8 discloses 2-(α-n-pentanonyl)benzoic acid.

6. It would have been obvious to a person of ordinary skill in the art at the time the invention was made to formulate the sodium salt of 2-(α-n-pentanonyl)benzoic acid, which is taught by STN Registry Number 550-37-8, to result in the instant compound. As taught by *Berge et al*, "The chemical, biological, physical, and economic characteristics of medicinal agents can be manipulated and, hence, often optimized by conversion to a salt form" (Page 1, Column 1, Paragraph 1). More specifically, *Berge et al* teach sodium as a potentially useful salt form approved by the FDA (Page 2, Table 1). Furthermore, *Yang et al* specifically teach the structurally and functionally related

compound  wherein n is 1 and M is the monovalent metal ion Na^+. Accordingly, it would have been obvious to a person of ordinary skill in the art to formulate the sodium salt of 2-(α-n-pentanonyl)benzoic acid in view of *Berge et al* - which provide a motivation to form salts forms of chemical compounds and which teach sodium as an acceptable salt form - and in view of *Yang et al* – which teach the sodium salt form of structurally and functionally related compounds.

7. Instant claims 25 and 26 are drawn to the compound of claim 1 for the treatment of cardio-cerebral ischemic diseases, etc and one or more pharmaceutically acceptable carriers (claim 25), in the form of a tablet, capsule, granule, etc (claim 26). *Yang et al* specifically teach that structurally similar 2-(α-hydroxypentyl)benzoates are useful in the "treatment of diseases such as cardioischemia, cerebroischemia, heart and brain arterial occlusions, etc" (Paragraph 0001). A person of ordinary skill in the art at the time the invention was made, recognizing the similarity in structure between the instant compounds and the compounds taught by *Yang et al*, would have expected the compounds would have similar properties and would have been motivated to use the compounds for the treatment of conditions taught by *Yang et al* with a reasonable expectation of success. Furthermore, *Yang et al* teach that “the pharmaceutical

composition of the present invention comprises a treatment effective amount of the compound of the present invention as an active ingredient and a pharmaceutically acceptable carrier" (Paragraph 0027). Additionally, *Yang et al* teach administration of the pharmaceutical formulation "in the dosage form such as tablets, particles, or capsules" (Paragraph 0030). Accordingly, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to formulate a pharmaceutical composition comprising 2-(α-n-pentanonyl)benzoate as an active ingredient and a pharmaceutically acceptable carrier, in the dosage form of a tablet (for example) to treat diseases such as cardio-cerebral ischemic diseases.

8. Applicant argues, however, that *Yang et al* "disclose that the preferred salt for hydroxypentyl compound is potassium, not sodium" (Applicant Argument, Page 4) and note that "the sodium salt is a sticky, yellow substance, which can only form a white amorphous foam, even after further treatment" (Applicant Argument, Page 5). Accordingly, Applicant concludes that "one of skill considering the art in its entirety would have considered the *Yang et al* disclosure to teach away from the use of the sodium salt in view of the relatively poor results compared to the potassium salt" (Applicant Argument, Page 5). Applicant's argument is not found persuasive. First, no where does *Yang et al* "disclose that the preferred salt for hydroxypentyl compound is potassium, not sodium" as asserted by Applicant. Furthermore, even *assuming arguendo* that *Yang et al* did include such a disclosure, as stated in *In re Susi*, "[a] known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use" (440 F.2d 442

(CCPA 1971) and, as stated in *In re Fulton*, "the prior art's mere disclosure of more than one alternative does not constitute a teaching away from any of these alternatives because such disclosure does not criticize, discredit, or otherwise discourage the solution claimed" (391 F.3d 1195 (Fed. Cir. 2004). In the instant case, nothing in *Yang et al* criticizes, discredits, or otherwise discourages the sodium salt of the compound.

9. Applicant also argues that it would be unpredictable to form salts of the present compound. Specifically, Applicant states that the free acid taught by STN Registry No. 550-37-8 is a colloidal solid after the solvent is removed, and thus "[a] person skilled in the art would recognize that if a colloidal solid is obtained after evaporating the solvent, the substance is an amorphous one" (Applicant Argument, Page 5). Although Applicant's argument is not clear, Applicant appears to suggest that the skilled artisan would not make a sodium salt of an amorphous substance. *Assuming arguendo* that solvent evaporation of colloidal solids in every case will provide an amorphous substance, Applicant provides no nexus between a substance being amorphous and forming a sodium salt of said amorphous substance. For example, as evidenced by *Pflaum* (WO 2001/10813), the sodium salt of pravastatin is present in an amorphous form (Page 2, Lines 24-27). Accordingly, Applicant's argument is not found persuasive.

10. Furthermore, Applicant argues that, although *Berge et al* teaches that an acid can be converted to a salt form, including a sodium salt, *Berge et al* also point out that "the preferred form is selected by pharmaceutical chemists primarily on a practical basis… there is no reliable way of predicting the influence of a particular salt species on the behavior of the parent compound." In support of this alleged unpredictability,

Applicant notes that *Yang et al* demonstrate "stark differences between the sodium and potassium salts of the hydroxypentyl compound" (Applicant Argument, Page 5). While Applicant is correct that *Berge et al* state that there is no reliable way of predicting the influence of a particular salt species on the **behavior** of the parent compound and that *Yang et al* demonstrate some differences between the sodium and potassium salts of structurally related compounds, formation of the sodium salt of a known compound would not be unpredictable even if some of its properties were unpredictable. In the instant case, however, Applicant has not established that the properties of the *prima facie* obvious sodium salt would have been unpredictable to a person of ordinary skill in the art. Specifically, Applicant argues that the skilled artisan would not have reasonably predicted that the instant compound "would have the good properties demonstrated here" (Applicant Argument, Page 5) such as good stability, a high melting point, good process ability such as flow ability, compressibility, comminuting ability etc, low acute toxicity, and good pharmacological effects (Applicant Argument, Pages 6-7). It is well settled that evidence of unexpected properties may be in the form of a direct or indirect comparison of the claimed invention with the closest prior art which is commensurate in scope with the claims (MPEP 716.02(b)III). In the instant case, Applicant's **(1)** provide data which indicate that 0.2 mg/ml sodium 2-(α-n-pentanonyl)benzoate in water showed less degradation between 1 and 24 hours when compared to the **potassium** hydroxypentyl compound taught by *Yang et al* (Specification, Paragraph 0051); **(2)** assert that "2-(α-n-pentanonyl)benzoates slightly absorbed moisture in a condition of certain humidity, but these salts almost may not be decomposed after absorbing

moisture, while **potassium** 2-(α-hydroxypentyl)benzoate was highly decomposed" (Specification, Paragraph 0056); **(3)** "solutions of various concentrations" of sodium 2-(α-n-pentanonyl)benzoate administered in a volume of 0.2 ml per 10 g body weight to mice showed reduced toxicity when compared to **potassium** 2-(α-hydroxypentyl)benzoate (Specification, Paragraph 0067); and **(4)** at a dosage of 50 mg/kg, MCAT rats administered 2-(α-n-pentanonyl)benzoate showed a statistical change in 24 hour behavioral scores compared to the Model group whereas rats administered **potassium** 2-(α-hydroxypentyl)benzoate did not (Specification, Paragraph 0077, Table 3); however at 100 mg/kg and 200 mg/kg, both groups showed as statistical change from the Model group (Tables 4 and 5). However, no where does Applicant compare sodium 2-(α-n-pentanonyl)benzoate to **sodium** 2-(α-hydroxypentyl)benzoate. And as to the comparison between sodium 2-(α-n-pentanonyl)benzoate and **potassium** 2-(α-hydroxypentyl)benzoate, Applicant does not provide data to establish that the alleged differences are statistically significant. As stated in *Ex parte Gelles*, the evidence relied upon should establish "that the differences in results are in fact unexpected and unobvious and of both statistical and practical significance" (22 USPQ 1318 (Bd. Pat. App. & Inter. 1992). One of ordinary skill in the art would have expected some differences between the compound taught by Registry No. 550-37-8, the sodium or potassium 2-(α-hydroxypentyl)benzoate taught by Yang et al, and the instant compound. There is nothing to indicate that the properties of the instant compound differ from the prior art to such an extent that the differences are really unexpected. Finally, it is noted that, even *assuming arguendo* that the differences

disclosed by Applicant were unexpected, Applicant's claims are not limited to the alleged unexpected results. Rather, the instant claims encompass, for example, compositions comprising any amount of sodium 2-(α-n-pentanonyl)benzoate with any pharmaceutically acceptable carriers whereas the unexpected results are limited to specific compositions.

Conclusion

No new ground(s) of rejection are presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CRAIG RICCI whose telephone number is (571) 270-5864. The examiner can normally be reached on Monday through Thursday, and every other Friday, 7:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/CRAIG RICCI/
Examiner, Art Unit 1614

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614